

What is claimed is:

5 *Sub 1*  
1. A method of measuring at least one parameter of a biological sample comprising the steps of:

(a) setting the temperature of said biological sample to a first temperature, said first temperature being within the physiological temperature range of said biological sample;

10 (b) performing an optical measurement on said biological sample at said first temperature;

(c) determining at least one optical parameter of said biological sample at said first temperature, said first temperature corresponding to a first depth in said biological sample;

15 (d) changing said first temperature of said biological sample to at least a second temperature, said at least second temperature being within the physiological temperature range of said biological sample;

(e) performing said optical measurement on said biological sample at said at least second temperature;

20 (f) determining said at least one optical parameter of said biological sample at at least a second temperature, said at least second temperature corresponding to a second depth in said biological sample; and

(g) determining said at least one parameter of said biological sample from the functional relationship of said at least one optical parameter on depth in said biological sample.

25  
2. The method of claim 1, wherein said change in temperature of said biological sample results in a change in penetration depth of light in said biological sample.

3. The method of claim 1, wherein said optical measurement is a diffuse reflectance measurement.

4. The method of claim 1, wherein said optical measurement is a spatially resolved diffuse reflectance measurement.

5. The method of claim 1, wherein said optical measurement is a frequency domain measurement.

6. The method of claim 3, wherein said diffuse reflectance measurement is performed at a single sampling distance.

7. The method of claim 1, wherein said first temperature and said at least second temperature are within a range from about 0 °C to about 45 °C.

8. The method of claim 1, wherein said first temperature and said at least second temperature are within a range from about 15 °C to about 45 °C.

9. The method of claim 1, wherein said optical measurement is performed using light at at least one wavelength in a range from about 400 nm to about 2500 nm.

10. The method of claim 1, wherein said optical measurement is performed using light at at least one wavelength in a range from about 600 nm to about 1300 nm.

11. The method of claim 1, wherein said at least one parameter of said biological sample is the concentration of an analyte.

Sub C1  
12. The method of claim 11, wherein said analyte is glucose, hemoglobin, or water.

5 13. The method of claim 1, wherein said at least one optical parameter is absorption coefficient, scattering coefficient, mean free path, effective attenuation coefficient, or light penetration depth.

14. The method of claim 1, wherein said biological sample is an excised tissue or a biopsy sample.

10 15. The method of claim 1, wherein said biological sample is a human body part.

16. The method of claim 1, wherein said biological sample is intact human skin, esophagus tissue, intestine tissue, or cervical tissue.

17. The method of claim 1, wherein said at least one parameter of said biological sample is a parameter indicating a disease state.

20 18. The method of claim 17, wherein said disease state is diabetic state, vascular disease state, dermatological disease state, or neoplastic disease state.

Sub A2  
19. A method of measuring at least one parameter of a biological sample having a plurality of layers, said method comprising the steps of:

25 (a) setting the temperature of said biological sample to a first temperature, said first temperature being within the physiological temperature range of said biological sample;

(b) performing an optical measurement on said biological sample at said first temperature;

Sub  
A 2 5  
(c) determining at least one optical parameter of a first layer of said biological sample, said first layer being located at a first depth of said biological sample, said first temperature corresponding to a first depth of said biological sample;

(d) changing said first temperature of said biological sample to at least a second temperature, said at least second temperature being within said physiological temperature range of said biological sample;

(e) performing said optical measurement on said biological sample at said at least second temperature;

10 (f) determining said at least one optical parameter at at least a second layer of said biological sample, said at least second layer being located at at least a second depth of said biological sample, said at least second temperature corresponding to said second depth of said biological sample; and

15 (g) determining said at least one parameter of said biological sample from the functional dependence of said at least one optical parameter on depth in said biological sample.

Sub  
OC 20  
20. The method of claim 19, wherein said change in temperature of said biological sample results in a change in penetration depth of light in said biological sample.

21. The method of claim 19, wherein said optical measurement is a diffuse reflectance measurement.

25 22. The method of claim 19, wherein said optical measurement is a spatially resolved diffuse reflectance measurement.

23. The method of claim 19, wherein said optical measurement is a frequency domain measurement.

24. The method of claim 21, wherein said diffuse reflectance measurement is performed at a single sampling distance.

25. The method of claim 19, wherein said first temperature and said at least second temperature are within a range from about 0 °C to about 45 °C.

26. The method of claim 19, wherein said first temperature and said at least second temperature are within a range from about 15 °C to about 42 °C.

27. The method of claim 19, wherein said optical measurement is performed using light at at least one wavelength in a range from about 400 nm to about 2500 nm.

28. The method of claim 19, wherein said optical measurement is performed using light at at least one wavelength in a range from about 600 nm to about 1300 nm.

29. The method of claim 19, wherein said at least one parameter of said biological sample is the concentration of an analyte.

30. The method of claim 29, wherein said analyte is glucose, hemoglobin, or water.

31. The method of claim 19, wherein said at least one optical parameter is absorption coefficient, scattering coefficient, mean free path, effective attenuation coefficient, or light penetration depth.

32. The method of claim 19, wherein said biological sample is an excised tissue or a biopsy sample.

33. The method of claim 19, wherein said biological sample is a human body part.

34. The method of claim 19, wherein said biological sample is intact human skin, esophagus tissue, intestine tissue, or cervical tissue.

35. The method of claim 19, wherein said at least one parameter of said biological sample is a parameter indicating a disease state.

36. The method of claim 35, wherein said disease state is diabetic state, vascular disease state, dermatological disease state, or neoplastic disease state.

37. An apparatus for measuring at least one optical parameter of a biological sample, said apparatus comprising:

(a) a means for irradiating a region of said biological sample with light;

(b) a means for collecting light re-emitted from said region of said biological sample,

(c) a means for changing the temperature of said biological sample to a temperature within the physiological range of said biological sample so that radiation penetrates to a specified depth in said biological sample,

(d) a means for measuring the intensity of the collected re-emitted light at a plurality of temperatures, wherein the measured intensities correspond to light re-emitted from different depths of said biological sample; and

(e) a means for calculating at least one parameter of said biological sample from the dependence of at least one optical parameter on depth in said biological sample.

38. The apparatus of claim 37, wherein said change in temperature of said biological sample results in a change in penetration depth of light in said biological sample.

39. The apparatus of claim 37, wherein said intensity of said collected re-emitted light is used to determine diffuse reflectance of said biological sample.

5 40. The apparatus of claim 37, wherein said intensity of said collected re-emitted light is used to determine spatially resolved diffuse reflectance of said biological sample.

10 41. The apparatus of claim 37, wherein said intensity of said collected re-emitted light is used to determine a frequency domain measurement of said biological sample.

15 42. The apparatus of claim 37, wherein said intensity of said collected re-emitted light is determined at a single sampling distance.

43. The apparatus of claim 37, wherein said temperature ranges from about 0 °C to about 45 °C.

20 44. The apparatus of claim 37, wherein said light used to irradiate said sample has at least one wavelength ranging from about 400 nm to about 2500 nm.

25 45. The apparatus of claim 37, wherein said light used to irradiate said sample has at least one wavelength ranging from about 600 nm to about 1300 nm.

46. The apparatus of claim 37, wherein said at least one parameter of said biological sample is the concentration of an analyte.

Sub  
C1

47. The method of claim 46, wherein said analyte is selected from the group consisting of glucose, hemoglobin, and water.

5  
Sub  
C1

48. The apparatus of claim 37, wherein said at least one optical parameter is selected from the group consisting of absorption coefficient, scattering coefficient, mean free path, effective attenuation coefficient, or light penetration depth.

10 49. The apparatus of claim 37, wherein said biological sample is selected from the group consisting of intact human skin, esophageal tissue, intestine tissue, or cervical tissue.

50. The apparatus of claim 37, wherein said at least one parameter of said biological sample is an indicator of a disease state.

15  
Sub  
A4

51. The apparatus of claim 37, wherein said disease state is selected from the group consisting of diabetic state, vascular disease state, dermatological disease state, and neoplastic disease state.

20  
Sub  
C1

52. The apparatus of claim 37, wherein said irradiation means and said temperature changing means are included in an endoscope.

add  
C1